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Non-Uremic Calciphylaxis? Ur-ine Trouble!

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Introduction/Learning Objectives

- Calciphylaxis manifests as painful skin lesions often seen in patients with End Stage Renal Disease
- One year mortality approaches 50%
- In rare circumstances patients without renal failure may develop calciphylaxis and prompt recognition is critical
- Treatment requires a multimodal approach focusing both on pain management and treatment of the underlying disease.

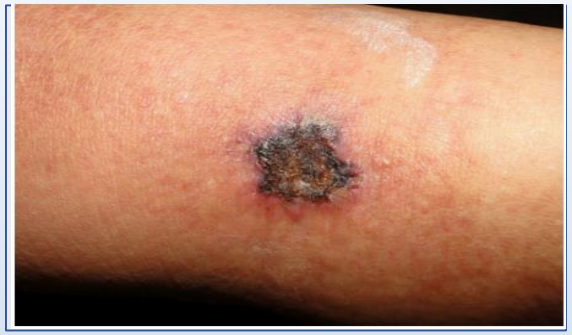
Case Presentation

- 48-year-old man with a history of alcohol abuse, dilated cardiomyopathy, heart failure with an ejection fraction of 25% and atrial fibrillation on apixaban presented with the complaint of painful, progressive skin lesions on his abdomen.
- The patient had a recent hospital admission 3 months prior due to cardiogenic shock requiring ICU admission during which he had acute kidney injury which resolved after treatment. Vital signs were within normal limits and he denied trauma.
- Physical exam was notable for obese body habitus and multiple 2-3 centimeter erythematous and purpuric patches with associated central ulceration and black crusting on the abdomen and proximal thighs.
- Punch biopsy of the subcutaneous adipose tissue revealed focal fat necrosis as well as scattered calcifications of small vessels, consistent with non-uremic calciphylaxis.
- The patient was started on sodium thiosulfate infusions, with dosing adjusted for the patient's heart failure, as well as sevelamer with modest improvement of skin lesions prior to discharge. His pain medication requirements remained high throughout the admission.

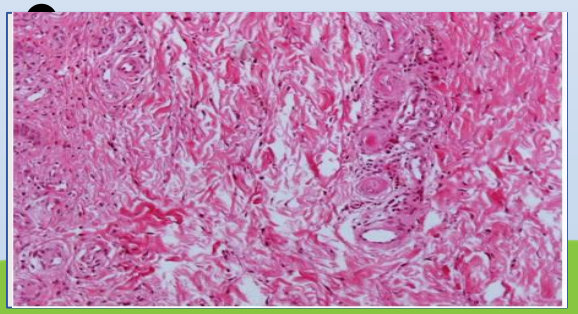
LABS

Creatinine: 0.82
Phosphate: 3.7
Calcium: 8.8
Parathyroid Hormone: 29

Antinuclear antibody: Negative
Cryoglobulins: Negative
Hepatitis C: Negative
Vasculitis Panel: Negative



Images from reference 1: Garcia-Lozano et al.



Email

Abstract

Discussion

- Calciphylaxis is characterized by painful skin lesions or subcutaneous nodules which often appear as plaques or livedo which develop a dusky discoloration and eventual ulceration, necrosis, and eschar formation.
- In patients with End Stage Renal Disease the diagnosis can be made clinically based on the appearance of the lesions. In other patients a biopsy is necessary to establish the diagnosis.
- Major risk factors for non-uremic calciphylaxis include obesity, hyperparathyroidism, diabetes, connective tissue or autoimmune disease, hepatitis, local trauma, and use of medications such as warfarin or excessive vitamin D.
- Complications include frequent hospitalization due to pain, prolonged wound healing, and infection. The one year mortality is estimated to be greater than 50% and typically results from sepsis secondary to wound infection.
- Sodium Thiosulfate is the most effective treatment for calciphylaxis and is typically administered in doses of 25 grams, three times weekly. The duration of therapy is unclear however response within the first one to two weeks appears to predict long term results.
- Adjunct treatments include surgical debridement, hyperbaric oxygen therapy, and bisphosphonates.

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Oral Contraceptives as Possible ACL Injury Prevention Method

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Abstract

Anterior Cruciate Ligament (ACL) injuries are an upsetting setback for many athletes that require a long and costly recovery process. The injury rates are four times greater in women than men. Preventative measures that help to prevent ACL injuries are limited to stretching and strengthening. Therefore, this review aims to investigate if oral contraceptive [I] usage provides a possible new avenue for prevention of ACL injury [O] in young female athletes (ages 18-30) [P] compared to those that do not take oral contraceptives [C].

Introduction

Anterior Cruciate Ligament (ACL) injury

Statistics

- ACL injury rates 4x > in F:M
- Roughly 200,000 tears per year in US as of 2017
- Reconstructive treatments= ~ $7.6 billion per year
- Rehabilitative treatments= ~ $17.7 billion per year

Physiology

- Estrogen has effect on collagen, altering its tensile properties of ligaments in ACL fibroblast
- Neuromuscular performance varies during the menstrual cycle
- Elevated serum relaxin-2 levels correlate with increased ACL injuries.

Current Prevention

- Stretching, strengthening, and mobility exercises aimed to release tension and tightness on the joint and strengthen muscles around the knee joint

Methods

Literature Search

- Performed in October 2018 using
  - PubMed
  - Google Scholar
  - SCOPUS
  - ClinicalKey
- Search Terms:
  - "ACL" AND "oral contraceptives"
  - "menstrual cycle" AND "ACL injury" AND "oral contraceptives"
  - "ACL injury" OR "joint laxity" AND "oral contraceptive".
- Inclusion Criteria:
  - Published in peer-reviewed journal
  - Published within last 10 years
  - Human participants as subjects
  - Female participants
  - Age range 18-30 y/o
- Exclusion Criteria:
  - Systematic reviews or meta-analyses
  - Male participants
  - Injuries other than ACL
  - Ages other than 18-30 y/o

Results

1. Arendt A., Bershadsky B. and Agel J. Periodicity of noncontact anterior cruciate ligament injuries during the menstrual cycle. The Journ of Gend Specif Med, 2002;5(2), pp.19-26.
- Retrospective cohort study of 83 participants aimed to compare the number of total ACL tears in females taking OCP vs not taking OCP over the span of 3 years

2. Gray A, Gugala Z, Baillageon J. Effects of Oral Contraceptive Use on Anterior Cruciate Ligament Injury Epidemiology. Medicine & Science in Sports & Exercise. 2016;48(4):648-654. doi:10.1249/mss.0000000000000806.
- Case control study of 347,118 participants designed to investigate what percent of OCP users underwent ACL reconstruction compared to non-users.

3. Hicks-Little C, Thatcher J, Hauth M, Goldfuss A, Cordova M. Menstrual cycle stage and oral contraceptive effects on anterior tibial displacement in collegiate female athletes. J Sports Med Phys Fitness. 2007;47(2):255-260.
- Case control study of 53 participants aimed to establish differences in anterior tibial translation in female athletes at varying stages of their menstrual cycles

4. Konopka J, DeBaun M, Chang W, Dragoo J. The Intracellular Effect of Relaxin on Female Anterior Cruciate Ligament Cells. Am J Sports Med. 2016;44(9):2384-2392. doi:10.1177/0363546516646374
- Laboratory experiment of 14 donors designed to investigate serum relaxin levels in estrogen-treated tissue samples compared to non-estrogen treated

5. Lefevre N, Bohu Y, Klouche S, Lecocq J, Herman S. Anterior cruciate ligament tear during the menstrual cycle in female recreational skiers. Orthopaedics & Traumatology: Surgery & Research. 2013;99(5):571-575. doi:10.1016/j.otsr.2013.02.005.
- Retrospective cohort study of 172 participants designed to find the distribution of ACL tears according to stage in menstrual cycle and oral contraceptive usage vs non-usage.

6. Martineau P, Al-Jassir F, Lenczner E, Burman M. Effect of the Oral Contraceptive Pill on Ligamentous Laxity. Clinical Journal of Sport Medicine. 2004;14(5):281-286. doi:10.1097/00042752-200409000-00006.
- Post-test control study of 172 participants designed to identify if there was a difference in joint laxity between OCP and non-OCP users by measuring KT-1000 measurements of anterior tibia translation

7. Nose-Ogura S, Yoshino O, Yamada-Nomoto K et al. Oral contraceptive therapy reduces serum relaxin-2 in elite female athletes. Journal of Obstetrics and Gynecology Research. 2016;43(3):530-535. doi:10.1111/jog.13226.
- Case control study of 106 participants designed evaluate serum-relaxin- 2 levels in OCP users vs non-users.

8. Rahr-Wagner L, Thillemann T, Mehnert F, Pedersen A, Lind M. Is the Use of Oral Contraceptives Associated With Operatively Treated Anterior Cruciate Ligament Injury?. Am J Sports Med. 2014;42(12):2897-2905. doi:10.1177/0363546514557240.
- Case control study of 4,497 participants designed evaluate percentage of OCP-users vs non-users in ACL tears, and furthermore, which percentage underwent reconstruction.

Study	Population Demographics	Control	Exclusion Criteria	Tx Compared	Outcome Measure
1	83 Females	Non OCP users	None	OCP users	% of ACL injuries
2	347,118 Females	Healthy age-matched female ACL (3:1)	History of hormonal disruptive condition, PCOS, hysterectomy, Turner syndrome, follicular/ovarian cyst, atrophy of ovary/fallopian tube, benign/malignant neoplasm of ovary, oophorectomy, pregnant state/ectopic in last 12 mo. Emergency contraception, implantable devices, hormonal IUDs, injectable/patch contraceptives	OCP users	% undergoing ACL repair
3	53 Females	Non OCP users	For control: no previous history of knee injury or anomalies and normal 28-30 day menstrual cycle	OCP users	KT-1000 measurements of anterior tibia translation
4	7 Males, 7 Females *F Ages: 19, 40, 20, 13, 46, 43, 20* *M ages: 36, 23, 26, 51, 20, 19, 26* *Race: Hispanic (1), White (10), American Indian (1), Asian (2)*	None	Prior ACL injury	Treated with concentrations of relaxin-2 or TGFβ1 or 17β-estradiol	MMP1, MMP3, MMP13, type I collagen, type III collagen, mRNA
5	172 Females *(mean age 34 +/- 8.7 years)*	Non OCP users	None	OCP users	% of ACL injuries
6	172 Females	None	None	OCP users	KT-1000 measurements of anterior tibia translation
7	106 Females *13 amenorrhea, 77 regular menstruation, 16 prior OC usage*	Non OCP users	Serum relaxin-2 < 6.0 pg/mL	OCP users	Hormone levels from blood samples (serum-relaxin 2)
8	13,355 Females *Median age=24 y/o*	Healthy age-matched female ACL (2:1)	For the controls: prior ACL injury	OCP users	% ACL injuries

collagenase-3

Discussion

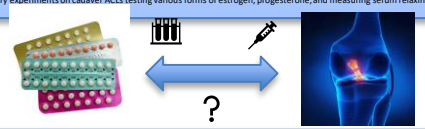
3/4 studies that analyzed % of ACL tear in OCP users vs non-users found less risk in OCP users; the other found no significant difference.

2/2 studies that measured anterior tibial translation in OCP users vs non-users found significantly less translation in OCP-users.

Strengths
- Statistically significant→ All utilized 2 methods of data analyses and all p value < 0.05
- 8/8 used inclusion/exclusion criteria, which resulted in decreased amount of confounding variables

Limitations
- Large differences in sample sizes
- Low external validity → none measured duration of OCP treatment nor described what type/strength of OCP
- None measured how long participants had been on OCP treatment
- Lack of long-term follow up

Future Research
- Inclusion/exclusion criteria applied in order to account for type/strength of OCP and duration
- Obtain information such as level of compliance and what day of the menstrual cycle the tears were on
- Obtain follow up and compare recovery rates in OCP users vs non-users
- More laboratory experiments on cadaver ACLs testing various forms of estrogen, progesterone, and measuring serum relaxin-2.



Conclusion

The study reveals a **significant difference in OCP-users vs non-users in terms of joint laxity and % of overall ACL tears**. Although there are limitations to some of this research, it provides a great blueprint for future studies and provokes some great ideas for clinical practice.

The determination of utilizing OCP in the future for ACL prevention **should be made on a case by case basis**. Potential contraindications such as personal or family history of breast cancer or clotting disorders must be taken into consideration.

Many questions and technical issues regarding how to best utilize OCPs must first be determined prior to bringing this into clinical practice- specifically, the **duration, form, and strength of the OCP usage**. This should be the **aim of future research.**

Until more research is performed and these questions are answered, it remains unclear if OCPs are a safe and effective preventative measure for ACL injury.. There is not yet enough evidence to safely utilize this in practice yet.

Overall, the meta-analysis reveals positive outcomes in utilizing OCPs as a preventative measure in ACL injury, but the evidence is insufficient to begin use in clinical practice.

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A Case of Macrophage Activation Syndrome in an Elderly Female

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INTRODUCTION

- Macrophage activation syndrome (MAS) is a rare but potentially fatal condition seen in association with certain rheumatologic disorders.
- In this case, we discuss a 74-year-old female with a complex past medical history who presented to the ED with fever and fatigue.

CASE

History of Presenting Illness:

•74-year-old female with a past medical history of scleroderma and ANCA-associated vasculitis with pauci-immune glomerulonephritis leading to ESRD on hemodialysis presented to the ED with fever and fatigue.

Initial Exam

- Vital Signs Temp 38.7C, HR 82, BP 132/70, RR 20, Sat 100% on room air
- Physical exam findings were notable for cachectic appearance with slight confusion, but without any neurologic deficits. No rash, or organomegaly.
- WBC 2400, Hgb 7.9, Platelets 212, BMP with notable Crt 3.06 but otherwise unremarkable.

Hospital Course

- The patient was evaluated for infectious, hematologic and neurologic etiologies.
- CT imaging revealed only a known chronic hematoma from prior kidney biopsy and MRI was without acute abnormalities.
- Lumbar puncture without significant findings, infectious workup negative.
- Rheumatologic labs were ordered given patient's pertinent history of autoimmune disease, particularly anti-SCL70 antibodies, which were consistent with her previous history of Scleroderma.
- Lab results were notable for ferritin 11,727 ng/ml, pancytopenia, elevated c-reactive protein 60.3 mg/L, elevated triglycerides 273 mg/dl, normal haptoglobin and low fibrinogen.
- During her hospitalization, she began to develop progressive altered mental status with rapid decline in cognitive functioning, confusion, and continued febrile episodes.
- In this setting, there were concerns for macrophage activation syndrome.

Treatment Regimen

•The patient was started on high-dose steroids with Solumedrol and daily Anakinra, an IL-1 Antagonist.

•Following initiation of treatment, there was notable progressive improvement of fevers, mental status, and lab abnormalities. Ferritin came down to 1047 ng/ml, triglycerides down to 60 mg/dl.

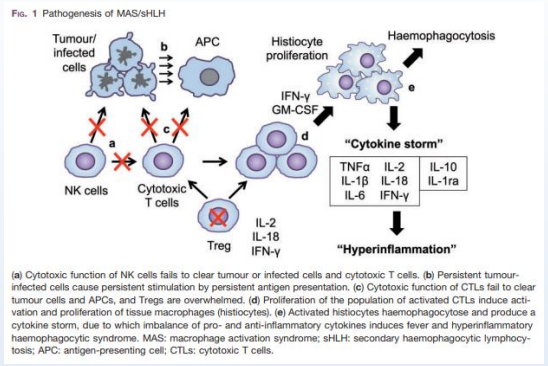
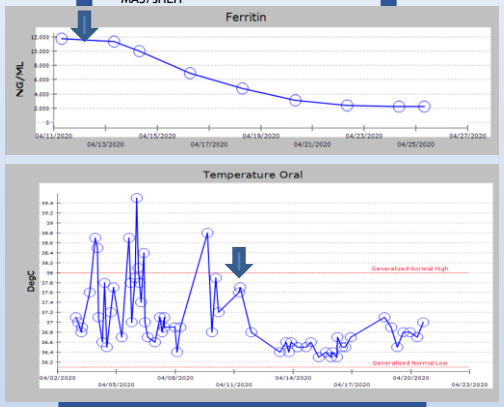


Fig. 1 Pathogenesis of MAS/sHLH

(a) Cytotoxic function of NK cells fails to clear tumour or infected cells and cytotoxic T cells. (b) Persistent tumour-infected cells cause persistent stimulation by persistent antigen presentation. (c) Cytotoxic function of CTLs fail to clear tumour cells and APCs, and Tregs are overwhelmed. (d) Proliferation of the population of activated CTLs induce activation and proliferation of tissue macrophages (histiocytes). (e) Activated histiocytes haemophagocytose and produce a cytokine storm, due to which imbalance of pro- and anti-inflammatory cytokines induces fever and hyperinflammatory haemophagocytic syndrome. MAS: macrophage activation syndrome; sHLH: secondary haemophagocytic lymphocytosis; APC: antigen-presenting cell; CTLs: cytotoxic T cells.

- Image 1 (above): Pathogenesis of MAS/sHLH [1]



- Image 2 (bottom): Ferritin and Temperature trend during admission, arrow indicates start of treatment

DISCUSSION

• The importance of the recognition of this relatively uncommon disease is important to ensure the appropriate treatment is started in a timely manner and to prevent further decompensation given its associated severity.

Pathogenesis

•MAS is also known as Secondary Hemophagocytic Lymphohistiocytosis (sHLH), although it is specifically termed Macrophage Activation Syndrome when associated with autoimmunity.

•Historically, MAS has been associated with adult onset stills disease and systemic idiopathic juvenile arthritis.

•Ebstein-Barr Virus in particular has been shown to be a trigger of MAS.

•MAS results in a cytokine storm leading to systemic inflammation with mental status changes and subsequent lab abnormalities distinct from Adult Onset Still's Disease including alterations in LFTs, Ferritin, LDH, Triglyceride, and d-dimer levels.

Diagnosis and Treatment

- First Line Tx is Corticosteroids- methylprednisolone, prednisolone, or dexamethasone
  - •Additional treatments include cyclosporine, IL-1 Receptor Antagonists (Anakinra), intravenous immunoglobulin (IVIG), cyclophosphamide, plasma exchange.

Prognosis

- Overall mortality is around 41%[1].
- Factors associated with poorer prognosis: substantially elevated serum ferritin level (in fact, a rapid rate of decrease in serum ferritin level by over 50% after treatment portends a lower risk of mortality), older age at onset, increased comorbidities, shock and severe thrombocytopenia at presentation.

Clinical Features of MAS	Laboratory Features of MAS
Non-remitting fevers	Cytopenia
Hepatomegaly	Abnormal liver function test
Splenomegaly	Coagulopathy
Lymphadenopathy	Decreased ESR
Hemorrhages	Hypertriglyceridemia
	Hyponatremia
	Hypoalbuminemia
	Hyperferritinemia

- Image 3 (above): Clinical and Lab features of MAS [1]

CONCLUSION

• Consider MAS when patient presents with fever, history of autoimmunity, with notable lab abnormalities including elevated triglycerides and ferritin, leukopenia, thrombocytopenia, elevated CRP, with normal to low haptoglobin, fibrinogen, and ESR.

•Start first line treatment with steroids or IVIG in steroid-refractory MAS. If there are features of established HLH, start Anakinra as a second line treatment. Anakinra has also been shown to be successful when used with steroids alone.

CITATIONS

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A Rare Finding of Sjögren-Induced Psychosis in an Adolescent Male

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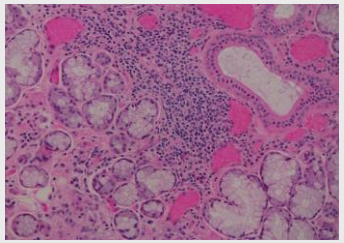
INTRODUCTION

Sjögren syndrome is a systemic autoimmune disorder resulting from focal lymphocytic infiltration of the exocrine glands with its primary phenotype causing dysfunction and diminished tear and saliva production, but additionally, can have other notable features. Sjögren syndrome affects 0.5% to 1.0% of the population and most commonly presents between the ages of 45 and 55. Worldwide, it primarily affects adults, and rarely children, with a female to male ratio of 9 to 1. It classically presents with sicca symptoms resulting from pathology of the lacrimal and salivary glands, though up to half those diagnosed also develop extra-glandular symptoms with joint, lung, gastrointestinal, nervous system, and kidney involvement. Very rarely, the literature has described cases of Sjögren syndrome presenting with psychiatric symptoms and with extensive research, exceptionally rare presentation in children.

CASE PRESENTATION

EHB is a 17 year old male with no significant past medical history who presented with several months of intermittent altered mental status, worsening auditory and visual hallucinations, and acute aggressive and manic behavioral changes. He was admitted for further evaluation with consults to Neurology and Psychiatry after initial stabilization in the PICU for agitation. His work up included EEG, EKG, and MRI of the brain, all of which were normal. Additional workup for organic etiology was obtained including autoimmune and infectious etiologies. Several autoimmune labs were found to be positive, including ANA and SSA/Ro antibody which prompted Rheumatology consultation for concern of possible Sjögren's Syndrome. Ophthalmology was consulted but Schirmer's test was negative for absence of tear production. Otolaryngology consulted for salivary gland biopsy which demonstrated some lymphocytic infiltration without granulomas which support diagnosis but is not confirmatory.

TREATMENT/RESULTS



EHB's salivary gland biopsy

Initially, patient demonstrated slight improvement with initiation of aripiprazole, but continued to endorse significant hallucinations and required frequent lorazepam for agitation. With concern for worsening psychosis and possible Sjögren's, patient was empirically treated with reduced pulse steroids (50mg/kg) for three days and experienced significant clinical improvement in mental status. He was noted to be more interactive with family and the care team, with improved mood and reduced hallucinations.

He began an oral steroid taper and hydroxychloroquine prior to discharge for presumptive Sjögren's and follow up was arranged with both Rheumatology and Psychiatry for close monitoring.

DISCUSSION

Rarely, Sjögren syndrome has been associated with psychiatric symptoms, including depression, anxiety, and psychosis. This presentation has only recently been described in the literature in a pediatric patient. A case series published by Hammett, E.K et al. in 2020 described four adolescent patients who presented with delusions, auditory hallucinations, severe anxiety, and altered mental status. These adolescents, ranging in age from 16 to 19 years, had laboratory findings consistent with Sjögren syndrome, including elevated ANA, and either elevated anti-SSA or anti-SSB antibodies similar to our patient. Additionally, all four patients lacked the classic finding of sicca, and three of the four had a normal brain MRI and EEG. All patients improved with initiation of treatment with steroids and Rituximab. The results of this study compelled us to further investigate the possibility of a diagnosis of Sjögren syndrome in our own patient.

DISCUSSION (CONT.)

Psychosis has numerous organic etiologies, including primary psychiatric disorders, as well as secondary causes of psychosis. Long-term management relies on careful evaluation to pinpoint the etiology at play. The extensive lab work obtained in our case allowed us to make an accurate diagnosis, and this changed our patient's prognosis and disposition entirely. Though there is utility in conducting a thorough work up in patients newly presenting with psychosis, it is also important to be thoughtful when obtaining extensive and often costly lab work.

CONCLUSION

We add to literature by presenting a very rare and unusual presentation of Sjögren's in a pediatric patient. Patients presenting with psychosis are likely underdiagnosed with organic underlying etiology, especially in children with no prior psychiatric history. This presents a need to rule out organic etiology in every patient as demonstrated by a significantly rare, albeit important, cause of psychosis in Sjögren Syndrome. However, careful consideration should be given to streamlining which diagnostics are used, often in parallel, as workups can be costly and time consuming as well as redundant. One consideration may be to streamline which diagnostics are sent in parallel (I.E. ANA alone), but also to have low threshold to rule out organic etiology with abrupt onset of new symptoms of severe psychiatric illness. Future management should be conservative and carefully planned in these instances in order to be cost-effective yet still allow delivery of quality, patient-centered and evidence-based care.

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Flu-minant Myopericarditis

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Introduction/Learning Objectives

#1: Over recent years, there has been an increase in the mortality associated with the Influenza virus, which has led to a higher number of hospital admissions for management of both the infection and its complications.

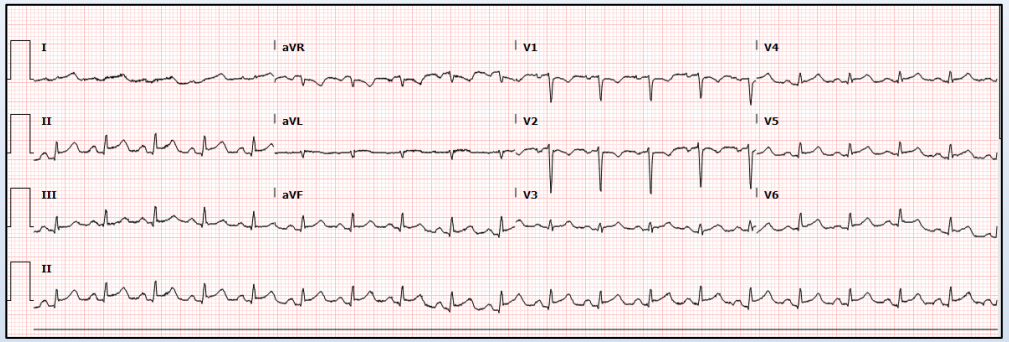
#2: Recognize potential complications associated with Influenza B.

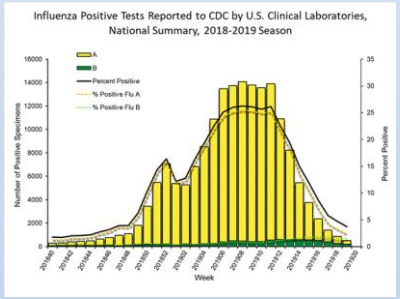
Case Report

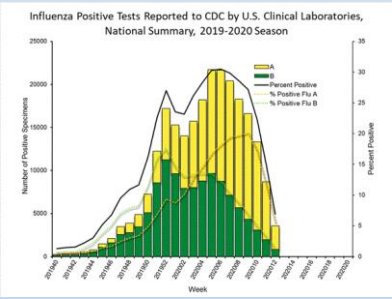
- **Patient:** 29-year-old female
- **Chief Complaint:** 5 days of body aches and fever associated with fatigue, chest tightness, diarrhea, vomiting, congestion and rhinorrhea
- **Past Medical History:** None
- **Initial Vital Signs:** HR 120
- **Labs:** lactate 5.2 mmol/L, WBC 10/nL, troponin 0.08 ng/mL with repeat 0.14 ng/mL, Respiratory Viral Panel positive for Influenza B
- **EKG:** diffuse ST elevations and PR depressions concerning for pericarditis
- **Echo:** moderate pericardial effusion, EF approximately 20%, concerning for cardiac tamponade physiology.
- **Interventional Cath Lab:** emergent pericardial window performed during which 180cc of straw-colored fluid was drained
- **Cardiac ICU**: within 2 hours cardiac function diminished with Fick cardiac output of 3.31 and cardiac index 1.71 - levels consistent with cardiogenic shock the setting of acute viral myopericarditis.
- The patient was immediately started on dobutamine, aspirin, and colchicine.
- Over the next 7 hours, the patient's cardiac output and index continued to deteriorate, requiring the initiation of milrinone as well as placement of an intra-rtic balloon pump.
- The patient was ultimately refractory to both inotropic and mechanical pport and was emergently initiated on ECMO.
- Due to continued hemodynamic instability despite these interventions, she was transferred to University of Pennsylvania for possible heart transplant.

Discussion Points

- **Influenza Infection Complications**
  - Pneumonia, ARDS, multisystem organ failure, myositis, rhabdomyolysis, CNS disease
- **Specifics of Cardiac complications**
  - EKG changes, acute myocardial infarction, myocarditis, pericarditis
- **Epidemiology of Influenza B**
  - There has been an increase in the prevalence of flu B
  - Previously shown to cause complications in pediatric populations but less often in adults
- **Future of Influenza research and education**
  - Further research is needed on the tropism of the Influenza virus
  - Education on vaccination and timely treatment of Influenza







Abstract

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Encapsulating Peritoneal Sclerosis, A Rare Complication of Peritoneal Dialysis

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Christiana Care

ABSTRACT

Encapsulating peritoneal sclerosis (EPS) is a rare and potentially life-threatening complication of peritoneal dialysis characterized by intraperitoneal inflammation and fibrosis. Mortality can be as high as 50% within 12 months of diagnosis. [1] An increased amount of time on peritoneal dialysis (PD), particularly over 5 years, is associated with developing EPS. The risk of occurrence after 5 years on PD is thought to range between 0.6 and 6.6%. [1] In patients undergoing PD for over 15 years the frequency of EPS may be as high as 17.2%. [2]

Cessation of PD, removal of the PD catheter, and switching to hemodialysis does not eliminate the risk of EPS since it has been reported to occur up to 5 years following PD withdrawal. It is important to mention that the majority of patients receiving peritoneal dialysis for a long period of time do not develop EPS. Hemodialysis carries its own risks including AV fistula failure (47% failure in year one), bacteremia, and endocarditis. [1] With the diagnosis of EPS patients are limited to treatments such as prednisone and tamoxifen. Surgery is reserved for severe EPS patients that present with bowel obstruction [3].

diarrhea. The patient had a significant past medical history of uncontrolled Hypertension, Diabetes since age 18 with proteinuria by age 24, noncompliance with medication and went on to develop End-Stage Renal Disease. Prior to her admission, the patient had been on peritoneal dialysis for 14 years. Initially, the patient was afebrile, hemodynamically stable.

PE: normal bowel sounds mild diffuse abdominal tenderness and mild distension. No lower extremity edema
Initial diagnostics: blood cultures negative.

Infectious peritonitis was initially suspected and intraperitoneal Vancomycin and Aztreonam were administered.

Over the next several days, she began experiencing waxing and waning fevers despite being on broad-spectrum antibiotics with worsening diffuse abdominal pain and persistent diarrhea.

Imaging:
CT Abdomen Pelvis with IV Contrast obtained showed a moderate amount of free peritoneal air and a small amount of ascites likely from peritoneal dialysis catheter and segmental mild wall thickening of the ascending, transverse and descending colon may reflect colitis.

Infectious colitis workup ultimately unremarkable which included but was not limited to CMV, C. diff, and enteric pathogens.
Peritoneal fluid dialysate analysis revealed cloudy fluid with elevated WBC, RBCs (bloody dialysate fluid), and neutrophil count > 50 which led to a diagnosis of peritonitis.

Intraperitoneal vancomycin and gentamicin washout therapy was initiated, however, the patient continued to experience diffuse severe abdominal pain with tenderness to palpation and diarrhea symptoms and no response to the antibiotics.

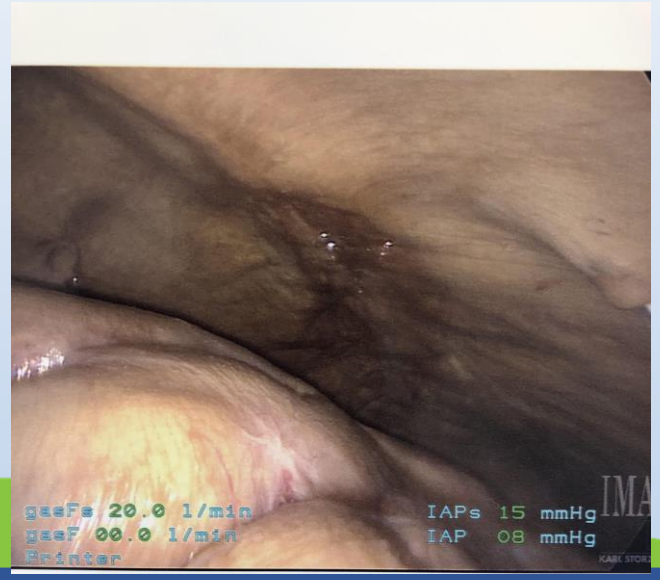
EGD with Colonoscopy was pursued to rule out inflammatory colitis and a potential source of vomiting which also was unremarkable. The patient was deemed to be **too high risk to go for a diagnostic laparoscopy** to rule out encapsulating peritoneal sclerosis.

However, during **laparoscopic removal of PD catheter**, general surgery noted **"diffuse sclerosing peritonitis on the abdominal walls as well as covering all the bowels"** No biopsies were taken. Due to these findings, the patient was given the diagnosis of Encapsulating Peritoneal Sclerosis. **Treatment with Tamoxifen and Prednisone was initiated.**

Conclusion

Encapsulating Peritoneal Sclerosis should be in a provider's differential diagnosis for patients who have a history of being on peritoneal dialysis for greater than 5 years, ultrafiltration failure, symptoms of ascites, and peritonitis that does not resolve with therapeutic measures such as paracentesis or antibiotics. CT of the abdomen may sometimes reveal a "thickened peritoneal membrane from the visceral to the parietal peritoneal surface, bowel tethering, localized or diffuse peritoneal calcification and encasement of the bowel." [3] The absence of these radiographic findings should not exclude the diagnosis of EPS. In order to rule out the diagnosis, a diagnostic laparoscopy with a peritoneal biopsy is required. On a pathology report, the typical findings are an organizing fibrosis within the peritoneum.

Image of EPS seen during removal of peritoneal dialysis catheter



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Cap-italizing on a novel therapy for acquired TTP for rapid platelet recovery

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BACKGROUND

- Thrombotic thrombocytopenic purpura (TTP) is a life-threatening microangiopathy caused by a deficiency of the metalloprotease, ADAMTS13.
- While mortality has been curtailed with medical advancement, mortality risk remains between 10-30%.
- Caplacizumab, a recently-approved monoclonal antibody for TTP, along with PEX and immunosuppressants, has the potential to further reduce this risk and improve patient outcomes.

CASE REPORT

22-year-old woman with no past medical history presented with one week of worsening shortness of breath and intermittent fevers.

- Associated symptoms: prolonged epistaxis, menorrhagia, bruising
- ROS: rhinorrhea, cough, headache, fatigue
- Family and social history: noncontributory
- No medication use

Physical Exam:

- HEENT: scleral icterus, pale conjunctiva
- Cardiac: tachycardic, regular rate and rhythm
- Skin: petechiae on dorsum of feet bilaterally, ecchymoses on upper thighs and arms

Laboratory Data:

- Hemoglobin 5.8, Platelets 9.0, WBC 11.7, Haptoglobin <8
- Total bilirubin 7.0, Direct bilirubin 0.8, AST 111, ALT 56
- Coagulation studies: within normal limits
- Troponin 0.06

ADDITIONAL LABS	
Respiratory viral panel	Rhinovirus
Blood smear	Schistocytes
ADAMTS13	<5%
ADAMTS13 inhibitor	3.2

Admission:
- Caplacizumab 1 mg daily IV

Day 2:
- Platelets increased to

Day 6 (Discharge):
- Blood counts re

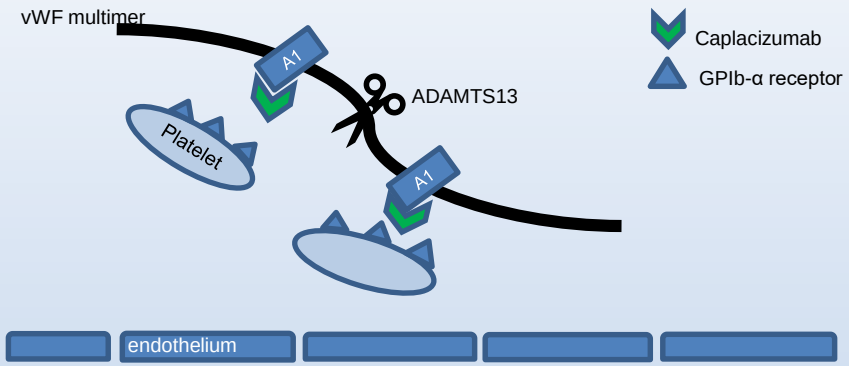
SCAN FOR E-MAIL

SCAN FOR ABSTRACT

DISCUSSION

- TTP is caused by deficiency of ADAMTS13, which cleaves von Willebrand Factor (vWF).
- Deficiency of ADAMTS13 results in abnormally large vWF molecules and widespread platelet aggregation.
- Plasma exchange (PEX) and steroids gold standard of care with mortality reduction of 29% (1).
- Caplacizumab binds to vWF A1 domain and antagonizes the platelet GPIb-α receptor, preventing platelet adhesion.
- Caplacizumab has been shown to be effective without plasma exchange as demonstrated in a case with a Jehovah's witness refusing PEX yet improved within 3 days of receiving caplacizumab (2).
- TITAN and HERCULES trials demonstrate ability of caplacizumab to promote rapid resolution of TTP and significantly decrease time to platelet count normalization, major thromboembolic events, and TTP-related deaths (3, 4).

CAPLACIZUMAB MECHANISM OF ACTION



CLINICAL IMPLICATIONS

- Initiation of timely PEX, immunosuppressants, and caplacizumab can drastically improve time to resolution of an acute TTP episode
- Adverse effects include bleeding, limited to epistaxis or gingival involvement. The most significant adverse events include gastrointestinal bleeds and hemorrhagic stroke.
- Future research needed to explore efficacy in various populations and long-term patient outcomes. Currently there is no set criteria to determine indications for this medication.

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Food Protein-Induce Enterocolitis Syndrome: An Under Recognized and Potentially Life Threatening Food Hypersensitivity

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INTRODUCTION

- Food Protein-Induced Enteroclitis (FPIES) is an under recognized and severe non-IgE mediated food hypersensitivity.
- Delays in diagnosis lead to unnecessary healthcare costs, significant morbidity, and even mortality.
- It is essential to raise awareness of FPIES among the medical community.

PATIENT PRESENTATION

ED PRESENTATION: A 6-month-old previously healthy male presented with acute onset of projectile and repetitive emesis, ptosis, head lag, lethargy, and unresponsiveness. Patient was breastfed and had recently begun introduction of solid foods. Three hours prior to symptoms, he ate sweet potato, banana, and oatmeal.

ED EXAM AND WORKUP: ML was lethargic and minimally responsive to pain. His vital signs were age-appropriate. CBC and CMP were remarkable for ALT 63, AST 93, and WBC 21. UA, UDS, EKG and CT Head were normal. IV hydration and empiric antibiotics were administered. Blood and urine cultures were ultimately negative. He had 5 additional witnessed episodes of vomiting and was admitted.

HOSPITAL COURSE: By 8 hours after admission, he was playful and back to normal activity. Repeat labs improved with normalized ALT, AST 48, and WBC 16. Additionally, EEG was normal. During monitoring, ML was exclusively breastfed and continued with normal accuchecks, vital signs, and exam. With negative workup, he was ultimately diagnosed with suspected severe, acute Food Protein-Induced Enterocolitis (FPIES) due to sweet potato, banana, or oats and discharged with plan to avoid these foods. Consultation with Allergy Immunology confirmed this diagnosis.

Figure 1: Most common food triggers include cow's milk, soy, rice, and oats.

DISCUSSION

FPIES is a severe non-IgE mediated food hypersensititivty that presents during the 1st year of life. It causes protracted emesis often with profuse diarrhea occurring a few hours after ingestion of an offending food. The incidence is about 0.28% in the United States, with a male predominance. The most common triggers are cow's milk, soy, rice, and oats, but also include a wide variety of foods. Local inflammation

DISCUSSION (continued)

in the GI tract is thought to be due to T cells, but the exact pathophysiology of FPIES is unknown.

Acute FPIES causes profuse vomiting, dehydration, lethargy, and hypovolemic shock. Chronic FPIES leads to intermittent vomiting, abdominal distention, anemia, and failure to thrive. Symptom resolution occurs with strict

DISCUSSION (continued)

avoidance of the culprit protein, and most children outgrow
it by age 3 or 4. If there is suspicion for FPIES, appropriate management includes stabilization, hydration, and simple avoidance of the culprit food.

Diagnosing FPIES can be a challenge as symptoms present 3 to 4 hours after ingestion of offending food, its presentation is variable, and diagnostic biomarkers are lacking. These patients often undergo full sepsis work ups, head imaging, antibiotic treatment, and hospitalization that are unnecessary and expensive. Some of these costs include head CT ($392-$2,015), EKG ($76-$240), lumbar puncture ($805-$1,270), and hospital admission (about $4,000/day). It is crucial to promote awareness of FPIES among emergency medicine physicians, intensivists, and inpatient hospitalists to minimize unnecessary costs, painful workups, and diagnostic delays.

CONCLUSIONS

- FPIES is potentially life threatening, under recognized, and warrants heightened awareness among the medical community.
- The differential diagnosis for an infant with extensive vomiting and lethargy often includes sepsis, intoxication, and head injury, but rarely includes a hypersensitivity reaction.
- The lack of awareness often leads to unnecessary healthcare spending on expensive and painful work ups.
- Without the correct diagnosis, proper counseling cannot be provided to families. This often results in additional ingestions of the culprit food leading to repeat of symptoms, additional workups, and significant morbidity, even mortality.

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[When] Endocrine Disorders Come in Twos

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Introduction

Autoimmune Polyglandular Syndrome Type II (APSII) is a combination of autoimmune adrenal insufficiency with autoimmune thyroid disease, as well as possible autoimmune diabetes mellitus[2]. This case describes a patient with a history of hypothyroidism, who presented with dyspnea on exertion, eructation, and nausea, found to be hypotensive and hyponatremic, and was diagnosed with primary adrenal insufficiency. We use this case to illustrate the importance of patient past medical history in aiding in the diagnosis of subsequent autoimmune pathology.

Initial Labs

113	84	25	
5.2	19	.96	96

15.2	
6.7	210

TSH: 46.87 MIU/L
Free T4: 1.0 ng/dL
Troponin: <0.01 ng/mL

Serum Osm: 240 MOSM/K
Urine Osm: 696 MOSM/K

U Na Random: 125 Mmol/L
U Crt 109.1 mg/dL

Discussion

This case illustrates the importance for high clinical suspicion of additional autoimmune pathology in a patient with a previous diagnosis of autoimmune disease, as 25% of patients with one autoimmune disease will go on to develop another [1]. As with our patient, the condition usually presents in middle-aged women, with incidence of 5 cases per 100,000 people in the US[2]. In 30% of APSII]patients, adrenal insufficiency emerges after autoimmune hypothyroidism or autoimmune diabetes. On the other hand, 50% of cases of APSII present with adrenal insufficiency as the initial abnormality, which can manifest with severe hypotension and volume depletion[2]. It was critically important for adrenal insufficiency to be recognized in this patient, albeit the inverse presentation of the syndrome, because adrenal insufficiency left untreated leads to a 1.5-2-fold increase in mortality[3].

Case Description

A 54 year-old female presented to the ED with five days of burping, dyspnea on exertion, intermittent hiccups, and some substernal chest tightness. She had tried simethicone and magnesium hydroxide without relief. Her husband had also noticed darkening of her skin complexion.

- **Past Medical History** - Anemia, Hypothyroidism, Major Depressive Disorder, ADHD
- **Social History** - Never Smoker, No alcohol or illicit drug use, works as a teacher
- **Surgical History** - Previous appendectomy
- **Allergies** - NKDA
- **Physical Exam** - VS: afebrile, HR 80s, BP 90s/60s, SpO2 100% in Room Air, AAOx3, and skin noted for increased pigmentation
- **Imaging** - EKG and Chest X-Ray were negative

Hospital Course

- The patient was admitted for management of severe hyponatremia
  In the setting of hypotension, severe hyponatremia, and hyperkalemia. there was a suspicion for adrenal insufficiency, and a morning cortisol was ordered with a result of 1.5 mcg/dL. Given her history of hyperpigmentation, it was further suspected that this was of primary origin, but a follow-up ACTH level was ordered. The ACTH result was 1155, confirming the diagnosis of primary adrenal insufficiency.
- The patient was managed with fluid restriction and hydrocortisone for her hyponatremia but also required D5W and Desmopressin to stabilize her sodium correction
- During her hospitalization, her Synthroid dose was also increased due to her increased TSH on arrival.

TABLE 1
Conditions Associated with Autoimmune Polyglandular Syndrome, Type II

CONDITIONS	PERCENT OF PATIENTS AFFECTED
Required for diagnosis	
Autoimmune adrenal insufficiency	100
Autoimmune thyroid disease	69 to 82
Type 1 autoimmune diabetes mellitus	30 to 52
Other associated conditions	
Vitiligo	4.5 to 11.0
Chronic atrophic gastritis, with or without pernicious anemia	4.5 to 11.0
Hypergonadotropic hypogonadism	4 to 9
Chronic autoimmune hepatitis	4

Figure 1.
A table of the conditions associated with Autoimmune Polyglandular Syndrome, Type II[2]

Figure 2.
Presenting symptoms of adrenal cortical insufficiency [3]

TABLE 2
Symptoms and laboratory changes in adrenal cortical insufficiency (AI)

Hormone	Symptoms
ACTH (POMC) stimulation (primary AI)	Hyperpigmentation
ACTH (POMC) suppression (secondary/tertiary AI)	Pale complexion
Glucocorticoid deficiency	Fatigue and decreased performance
	Appetite / Weight loss
	Nausea, vomiting, and abdominal pain
	Myalgias and joint pain
	Orthostatic hypotension
	Anemia, lymphocytosis, eosinophilia
	Hypoglycemia / hypoglycemic tendency
	Hyponatremia (no inhibition of ADH secretion)
	Hypercalcemia
	Slight TSH increase
Mineralocorticoid deficiency (primary AI)	Hypotonia, hypovolemia, creatinine increase, orthostatic dysregulation
	Hyponatremia
	Hyperkalemia
	Salt hunger
Androgen deficiency	Loss of axillary and pubic hair (females)
	Dry skin (females)
	Depression, loss of libido (females)

ACTH, adrenocorticotropic hormone; ADH, antidiuretic hormone; POMC, proopiomelanocortin; TSH, thyroid stimulating hormone

Key Points

This case serves to highlight that although a high number of patient will present with adrenal insufficiency as the first condition in Autoimmune Polyglandular Syndrome Type II , clinical index of suspicion should remain high to continue follow=up for patient who present with another endocrine disorder, such as Type I diabetes or autoimmune thyroid disease.

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Adult Still's Disease: Macrophage Activation Syndrome Secondary to Mycoplasma Pneumoniae

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Maryah Mansoor, MBBS, Rheumatology, ChristianaCare

CASE PRESENTATION

A **40-year-old** male presented to the hospital with…

- nausea, vomiting, and diffuse abdominal pain for 2 days
- fevers, arthralgias, and dry cough for 2 weeks
- medical history of **juvenile idiopathic arthritis** (JIA).
- **febrile to 39.7 C, mildly hypoxic, ill-appearing, with a blanchable, erythematous rash** on his back and arms.
- chest, abdominal, and pelvic **imaging was unremarkable**

WBC	2.5 L
Hgb	11.3 L
AST	721 H
ALT	540 H
ALP	221 H
TRIG	405 H

Platelet	188
Ferritin	>100,000 H
CRP	11.3 H
Fibrinogen	153 L
RF	<10 L
ANA multiplex	Negative

- urinalysis, respiratory viral panel, hepatitis panel, stool enteric pathogens and blood culture were negative
- **negative labs:** CCP, ASMA, AMA, ceruloplasmin, hemochromatosis HFE gene, and alpha 1 antitrypsin tests, EBV, CMV, tick-borne viruses, hantavirus, fungal and tuberculosis tests

Mycoplasma pneum IgG	Positive
Mycoplasma pneum IgM	Reactive

LEARNING POINTS

- **Diagnose** Adult Still's disease complicated by macrophage activation syndrome
- **Recognize** M. pneumoniae as a potential trigger
- **Utilize** an effective treatment regimen including an IL-1 antagonist

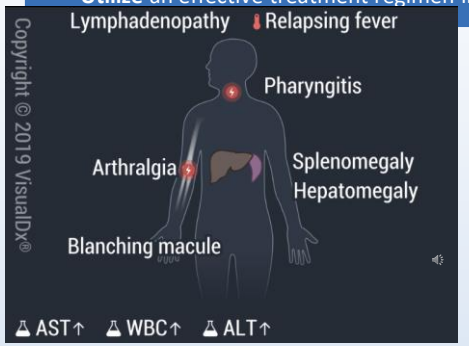

FIGURE 1: Signs and symptoms of ASD. Image is from VisualDx.

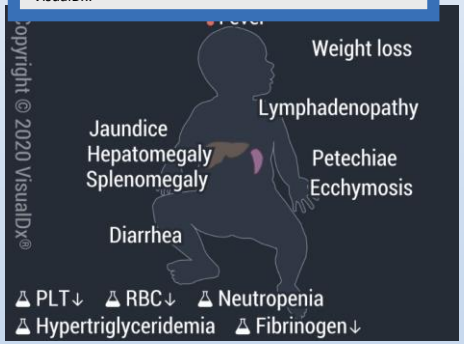

FIGURE 2: Signs and symptoms of MAS; more often seen in pediatric than adult patients. Image is from VisualDx.

Table 1: Clinical Diagnostic Criteria for ASD requires 5 or more criteria met, with at least 2 major criteria met

Major criteria	• **Fever** > 39 C for at least 1 week • **Arthralgia** or arthritis for at least 2 weeks • Nonpruritic salmon-colored **rash** on trunk/extremities • Granulocytic leukocytosis (10,000/microL or greater)
Minor criteria	• Sore throat • Lymphadenopathy • Hepato- or splenomegaly

Table 2: Classification Criteria for MAS. A febrile patient with known or suspected systemic JIA is classified as having MAS with the following labs

Must have	• **Ferritin >700 ng/L**
AND at least 2 of the following	• Platelets <180 x 109/ml • **AST >50 U/L** • **Triglycerides >160 mg/dL** • **Fibrinogen <360 mg/mL**

DISCUSSION

Adult Still's Disease (ASD)

- presents as daily fevers, arthralgias, rash, leukocytosis, elevated ferritin
- may include cardiopulmonary involvement, liver disease, abdominal pain and nausea
- is a **diagnosis of exclusion**, alternative systemic rheumatologic diseases, malignancy, infection, and drug reactions must be ruled out[4]

Macrophage Activation Syndrome (MAS)

- is a form of hemophagocytic lymphohistiocytosis
- **is a severe complication** that occurs in a minority of JIA
- **typically seen in pediatrics**, MAS rarely occurs in adults.
- ↑CRP, anemia, and leukopenia
- prompt treatment is critical as MAS is life threatening
- viral infection is the most common trigger
- **M. pneumoniae**, has been reported in few childhood MAS cases and in one ASD case report

Treatment:

- **pulse dose steroids**, Bactrim, and doxycycline, **IL-1 antagonist, Anakinra**
- symptoms and labs drastically improved
- stable for discharge by day 8 with outpatient rheumatology follow-up

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DISCLOSURE: There are no financial conflicts for any of the authors.

ChristianaCare™

A Rare Case of *Aerococcus urinae* Infective Endocarditis

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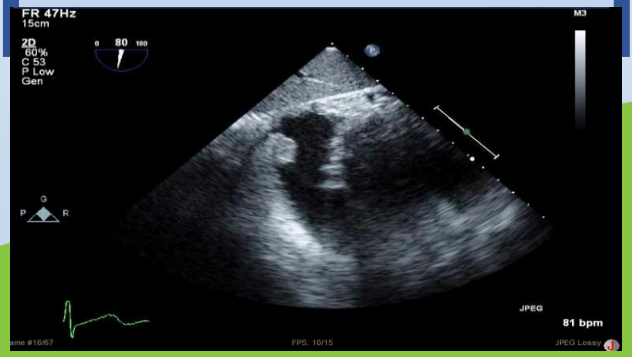
INTRODUCTION

- ✓ *Aerococcus urinae* is a gram positive bacterium and a rare pathogen previously thought to be a urinary contaminant lacking clinical significance
- ✓ First reported in 1967, the organisms belonged to a loosely associated bacterial group referred to as *Aerococcus*-like organisms
- ✓ This group—previously found in breweries, meat-curing brines, lobsters, and horse urine—caused urinary tract infections
- ✓ Since discovery, several UTI studies estimate A. urinae incidence as 0.15–0.8%, likely an underestimate due to misclassification of A. urinae for Staphylococcus, Streptococcus, or Enterococcus`
- ✓ *Aerococcus urinae* is also a rare cause of



CASE REPORT

- ✓ 71 y/o male with a past medical history of obstructive sleep apnea on CPAP, hypertension, Parkinson's disease, benign prostatic hyperplasia requiring intermittent catheterization for urinary retention, and recurrent *Aerococcus* urinary tract infections who presented with concerns of acute encephalopathy
- ✓ He had a urinalysis that was positive for leukocyte esterase and was subsequently reflexed to urine culture, which was positive for both *Enterococcus faecalis* and *Aerococcus urinae* and was initiated on Ampicillin and diagnosed with bacterial prostatitis
- ✓ Patient was starting to feel febrile, thus blood cultures were checked and were positive for *Aerococcus urinae* as well
- ✓ Noted some transient shortness of breath thus, in conjunction with positive blood cultures, had a 2D Echocardiogram that showed a 0.8 cm vegetation on his aortic valve
- ✓ Given these findings, Infectious Disease was consulted and synergistic Gentamicin was added on for treatment
- ✓ A transesophageal echocardiogram was ordered and showed a 1.12 x 1.01 cm vegetation on the ventricular side of the aortic valve
- ✓ To ensure that there was no mycotic aneurysm as a potential complication, he had an MRI brain and CTA of his head which were unremarkable
- ✓ A PICC line was placed so that he was able to get IV antibiotics (Ampicillin + Gentamicin) for 6 weeks with weekly monitoring of his BMP and Gentamicin trough

DISCUSSION

- ✓ Currently, there are no guidelines from the IDSA regarding treatment of *Aerococcus* endocarditis given its rarity
- ✓ Tathireddy et al. notes that most of the cases published regarding *Aerococcus* infectious endocarditis utilize penicillin based antibiotics with synergistic Gentamicin for a period of 6 weeks, however optimal treatment has not been determined
- ✓ In the present case, our patient's mental status improved after receiving ~1 week of Ampicillin and Gentamicin further demonstrating the utility of utilizing penicillin based antibiotics with synergistic Gentamicin
- ✓ Although 2D Echocardiography is not routinely recommended in UTIs, the outcome of this case does illustrate the utility of Echocardiography when a patient is bacteremic with *Aerococcus urinae*

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A CASE OF KEYTRUDA-ASSOCIATED MYOSITIS

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OBJECTIVES / PURPOSE

- Recognition of a patient presenting with Keytruda associated myositis
- Describe high-mortality side effects associated with Keytruda

CASE PRESENTATION

An 81-year-old woman presented to the hospital with weakness and chest pain

- History of metastatic hepatocellular cancer on pembrolizumab (Keytruda) - received last dose 3 weeks prior to presentation
  - 3 weeks of progressive, painful, bilateral & proximal limb-girdle weakness
  - 1 day of sharp substernal chest pain without radiation or exacerbating factors; self-resolved
  - No fevers, rashes, bowel/bladder dysfunction; ROS otherwise negative
- Exam: chronically ill appearing woman with unremarkable vitals, HEENT, heart, lung and abdominal examination. No skin rashes were found.
- Neuro exam:
  - Normal cranial nerves; strength was ⅗ at hip; ⅕ in the shoulder girdle; 5/5 distally
  - No sensory deficits, 2+ reflexes throughout, toes were down-going. No tremors/fasciculations, rigidity
  - She could not complete gait testing.
- Labs:

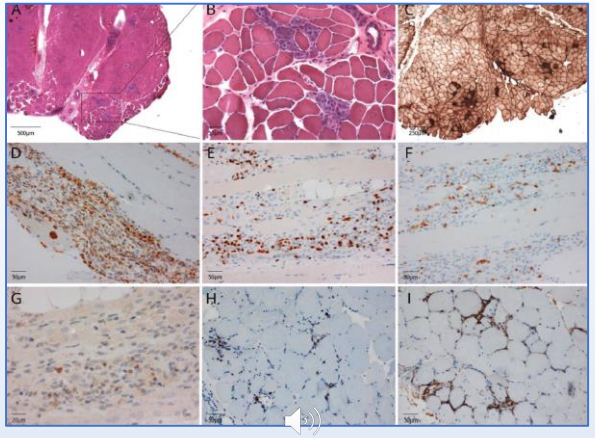
140	103	12	71
4.6	27	0.95	

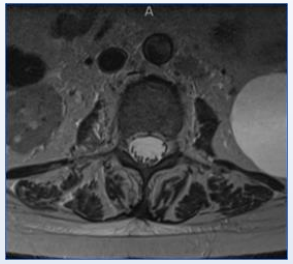
Mg – 2.1
Phos – 2.8
Ca – 8.4

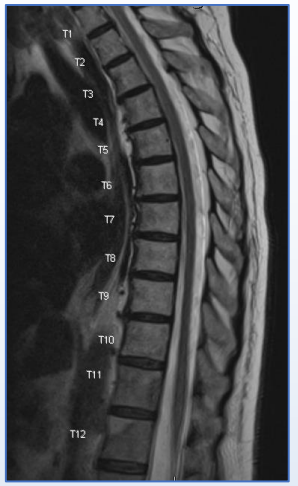
	9.7	
8.7		244
	33.1	

CRP – 57
ESR – 82
TSH – 2.8
Troponin - < 0.01 x 2
Respiratory viral panel – negative
Novel 2019 coronavirus - negative

- Imaging:
  - Chest x-ray normal; EKG non-ischemic
  - Thoracic/lumbar MRI: redemonstrated metastatic disease without nerve compression implicating dysfunction at the muscle level.
    - Edema at paraspinal, psoas & iliacus muscles
- The patient was treated as Keytruda associated myositis with high-dose oral prednisone and statin was held.
- Within a few days, the patient's strength recovered to near baseline ambulatory status and the patient was discharged to home hospice.







DISCUSSION

- Immune checkpoint inhibitors (ICIs) are a class of drugs that stimulate an anti-tumor immune response and have proven to be efficacious cancer therapy.
  - Keytruda, a type of ICI, is a humanized monoclonal programmed death-1 antibody that blocks the interactions between T-cells and tumor cells, thus reversing T-cell exhaustion.[1]
- ICIs have known adverse effects, including cutaneous, hematologic and endocrine abnormalities.
  - A less common side effect is immune-mediated myositis, occurring in < 1% of patients on ICIs[2].
  - Keytruda is less frequently associated with myositis compared to other ICIs[3].
  - Patients may also present with asymmetric ptosis, dysphonia, dyspnea associated with CK levels over 1,000.[3]
- Although our patient's chest pain workup was negative, it is important to note that patients may present with myocarditis. This is an uncommon but potentially fatal adverse consequence of ICIs.[4,5]

CONCLUSION

- Hospitalists should consider ICI-induced myositis in patients with muscle weakness in the proximal muscle distribution, especially presenting in the weeks after administration.
- In all patients suspected of ICI myositis, the agent should be immediately stopped, CK levels and cardiac functioning should be monitored. Steroids should be initiated as soon as possible.

Increased awareness of the less common side effects of ICIs, such as myositis and myocarditis, will allow early detection and initiation of treatment, thereby reducing the morbidity and mortality in these patients.

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Melena, Anemia and Critical Aortic Valve Stenosis: Is this Heyde Syndrome?

Clinical Vignette

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FOR THE LOVE OF HEALTH

Introduction

Heyde Syndrome is a rare condition characterized by bleeding in the GI tract due to Arteriovenous malformations (AVMs) in the setting of critical Aortic Stenosis (AS) that causes von Willebrand Syndrome (vWS) type 2A and resultant coagulopathy.

Case Description

94-year-old female with PMH significant for CHF and HTN presented with c/o melanotic stools for 1-2 wks, DOE and increased fatigue. VSS except for soft BP at 95/43 mm hg, PE: Grade 3/6 systolic murmur and benign abdominal exam..

Labs : Hgb at 6.3, MCV at 85.7, PT -13.1 sec, and PTT -28, INR -1.2 , NT Pro BNP - 1397. CTA of the abdomen and pelvis - Negative. EGD: Benign appearing esophageal stenosis and large hiatal hernia. Unable to visualize majority of stomach or duodenum due to significant hiatal hernia and looping. Noted to have 1-2 small non bleeding AVMs.

2D Echo: critical AS. She continued to have melanotic stools requiring multiple blood transfusions. Deemed to be high risk for repeat endoscopic procedures due to critical aortic stenosis. . Bleeding scan suggestive of active bleed in the left upper quadrant adjacent to splenic flexure, however STAT follow-up with repeat CTA of the abdomen and pelvis was negative. VIR unable to intervene unless she has a positive CTA study, to better localize the site of bleeding. GI unable to perform repeat EGD or colonoscopy due to increased cardiovascular risk and they raised concern for Heyde Syndrome. Seen by Hematology, had lab work done. Factor VIII was noted to be high at 375%. VWF Activity was above normal at 157% and VWF Antigen was high at 192%. VWF Multimers report revealed low to absent High Molecular Weight Multimers (HMWM) but no definitely increased abundance of lower molecular VWF multimers suggesting an acquired abnormality of VWF multimers. Per Cardiology recommendations patient successfully had TAVR done. Hemoglobin remained stable post TAVR and she was discharged home. Advised follow up with GI for outpatient colonoscopy and possible repeat EGD. At post discharge follow-up one week after TAVR patient had no new episodes of melanotic stools or signs and symptoms of bleeding.

Discussion

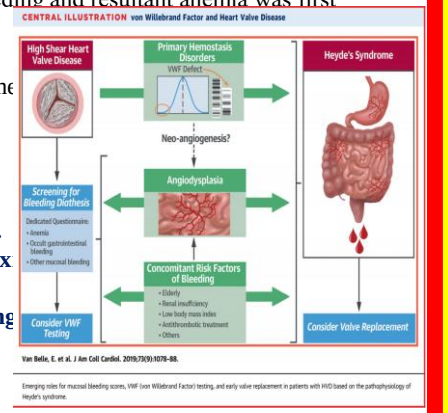
The association of critical AS with AVM's causing GI bleeding and resultant anemia was first published by Heyde in 1958.

In the setting of severe AS there are 2 main pathophysiological changes that contributes to this syndrome

1. AS leading to the development of AVMs

Theories :

- **AS can cause chronic low grade colonic hypoxia → reflux vasodilatation and relaxation of smooth muscles of the vessel → Ectasia of the blood vessel.**
- **→ Alteration in pulse wave → colonic mucosal Hypox**
- **→ cholesterol emboli from Aortic valve**
- **Angiodysplasia could be a result of aging and bleeding from these sites can be from acquired vWS .**



2. AS causing vWS type 2A

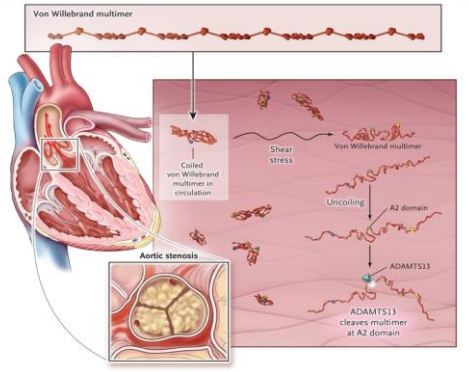
(an acquired deficiency of HMW vWF multimers)

VWF are produced by endothelial cells and circulate as large multimers. When they pass through stenotic aortic valve, high sheer force cause change in the conformation of the multimers, exposing A2 domains, that can be broken by ADAMTS 13 enzyme → decrease in size of HMW multimers and these are hemostatically less active - → Increased risk for bleeding.

Aortic Valve Replacement (AVR) provides cure for Heyde syndrome as it has shown to improve coagulation abnormalities by improving HMW multimers. TAVR is a better option to these patients as most of them are elderly and may have other comorbid conditions which could put them at high risk for surgical aortic valve replacement.

Conclusion

- **Heyde syndrome should be considered as one of the differentials in patients with recurrent unexplained GI bleeding or Iron deficiency anemia in the setting of Aortic stenosis.**
- **AVR can cure Heyde syndrome.**
- **Identification of this issue and appropriate management with AVR can improve patient's quality of life and prevent rehospitalization related to GI bleeding or Anemia.**



Avoiding Premature Closure: Chronic Fatigue, an Abdominal Mass, and a Diagnosis of HIV

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INTRODUCTION

•Search satisfaction bias, or anchoring, is pervasive in clinical practice and can be a deadly source of diagnostic error.[1]

•Anchoring refers to the practice of affixing to an early diagnosis despite new evidence indicating there may be an alternative explanantion.[2] This if often the result of unchecked Type-1, or intuitive, processing.

•Physicians who exhibit anchoring bias have been shown to commit diagnostic errors at a higher rate than even those displaying many of the other cognitive biases commonly associated with medicine.[3]

•By critically evaluating our intuitive decisions with Type-2, or analytical, thinking, such premature closure can be avoided.

CASE DESCRIPTION

•A 64-year-old man presented to the emergency department with complaints of worsening fatigue and weight-loss.

•Similar complaints had brought him to the ED 3 times in the previous 6 months, with negative workups and instructions to follow up as an outpatient, though he never did.

•However a CT scan was obtained due to the complaint of abdominal pain which revealed an 8 x 8 cm mass in his abdomen with associated lymphadenopathy.

•The radiologist's impression was possible neoplasm which needed further evaluation.

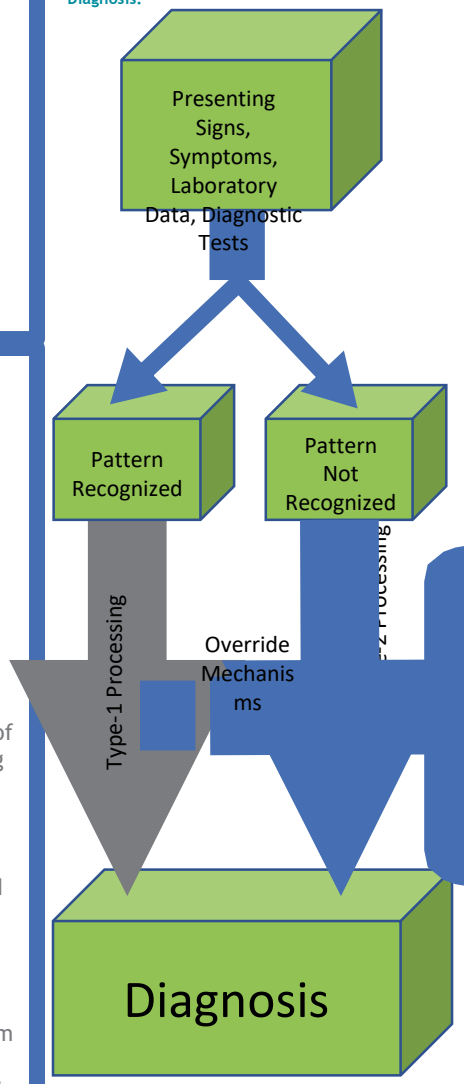
•The hospitalist admitted the patient. Notably, they did so not only for workup of the mass, but also for further evaluation of his fatigue and weight-loss, including testing for Human-Immunodeficiency Virus (HIV).

•After initial consultation with oncology the decision was made to biopsy the mass. Interventional radiology attempted a biopsy few days later at which time the mass was no longer visible. Repeat imaging confirmed resolution of what had likely been a small bowel intussusception.

•In the interim, the patient was found to be HIV positive thanks to the testing ordered by the admitting hospitalist.

•A more thorough history was obtained and revealed a partner who had died from complications of HIV 15 years prior. With the first presumptive cause of his fatigue and weight-loss ruled out, and a different etiology identified, the patient was discharged to follow up at the HIV clinic.

FIGURE 1. Simplified Model of Medical Diagnosis.



Adapted from *Croskerry P. A universal model of diagnostic reasoning. Acad Med. 2009;84(8):1022-1028. doi:10.1097/ACM.0b013e3181ace703*

DISCUSSION

•At this presentation it would have been easy to assume the "mass" seen on imaging, seemingly consistent with a malignancy, was the root cause of these symptoms.

•Diagnostic failure has been estimated to transpire in 10 to 15% of all medical cases, with Type-1 heuristic-type processing often to blame.[4,5]

•The admitting physician likely had Type-1 thinking initially, writing the patient's fatigue was "likely related to [the] new findings of mass."

•To decouple from Type-1 thinking, there are Type-2 processing mechanisms that can be employed to override intuitive thinking.[3]

•By subconscious or conscious use of these strategies, the admitting hospitalist obtained further studies in case the mass was not the answer, which in the end facilitated arrival at the patient's correct diagnosis.

possibilities
- Building a differential every time

Metacognition: Examining your own thinking processes
- Step back from question at hand

Lessen Dependence on Memory: Improving the accuracy of Judgements
- Make use of mnemonics, guidelines, and algorithms

Engage in Training: Directed Learning to Employ Analytical Thought

SOURCES

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Carotid bruit as the only sign of critical large-vessel atherosclerosis

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Objective

- Recognize the insidious nature of cerebrovascular events
- Highlight risk factors and physical exam findings of cerebrovascular events

Introduction

- Strokes from carotid stenosis account for a relatively small number of strokes[1]
- Critical atherosclerosis can occur even in relatively healthy patients with well-controlled risk factors

Patient Presentation

85-year old Caucasian male with past medical history of hypertension and hyperlipidemia well-controlled with medication

- Two-day history of right-sided hemiparesis, ataxia, and vague visual disturbances
- Symptoms completely resolved 1 day after admission
- At baseline, patient is independent and active, able to mow the lawn without assistance and remind his wife of appointments

Medications

Aspirin, atorvastatin, hydrochlorothiazide

Physical Exam

HR: 63 - RR: 17 - BP: 160/74 - Temp: 36.4 °C - Pulse Ox: 98% RA

General: Pleasant elderly male lying in bed in no acute distress, alert and oriented x3

Neurologic: Trouble with rapid alternating movements in upper extremities. Slow finger to nose on right side. Trouble walking heel-to-toe. Neurologic deficits resolved 1 day after admission.

Cardiovascular: Regular rate and rhythm. 2/6 systolic bruit. **Soft carotid bruits bilaterally L >R**

Laboratory Tests

CBC and CMP within normal limits

Glucose (nonfasting): 106

HbA1c: 5.2%

Lipids

- Cholesterol: 166
- HDL: 71
- Triglycerides: 54
- LDL: 84

Imaging

- Echocardiogram: mild to moderate aortic stenosis. No evidence of patent foramen ovale or shunt
- CT head without contrast: nonspecific white matter hypodensities most likely representing chronic small vessel disease. No evidence of intracranial bleed or infarct
- **MRI/MRA head and neck: multiple embolic infarcts in the bilateral frontoparietal and occipital lobes. MRA demonstrated 90% stenosis of the cervical internal carotid artery on the left and 70% stenosis on the right, 70% stenosis of the bilateral carotid bulbs and proximal internal carotid arteries, as well as 80**

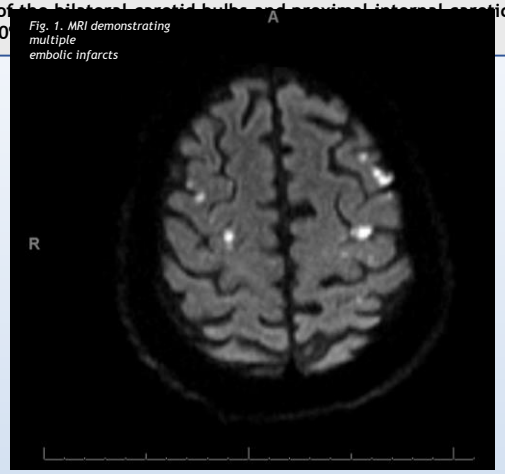

Fig. 1. MRI demonstrating multiple embolic infarcts

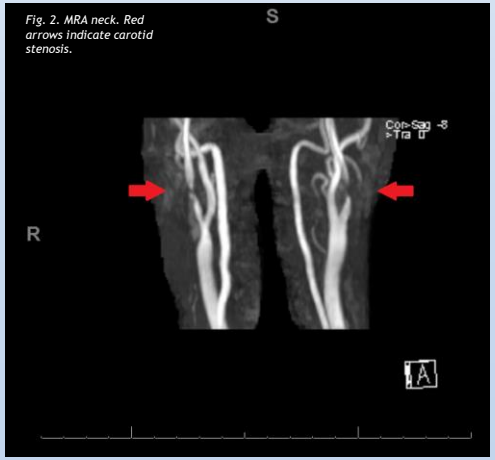

Fig. 2. MRA neck. Red arrows indicate carotid stenosis.

Next Steps

- Patient immediately placed on dual antiplatelet therapy and transferred to the stroke unit
- Left carotid endarterectomy performed without complications
- Discharged two days after surgery. Patient had no residual symptoms and reported feeling at baseline

Discussion

Risk factors for atherosclerosis

- **Age**
- **Hypertension**
- **Dyslipidemia**
- Smoking
- Diabetes
- Overweight
- Family history

- Atherosclerosis is an insidious process that's difficult to detect
- Carotid stenosis >50% is present in 7% of men and 5% of women over 65[2]
- USPTF currently does not recommend screening in any patients, including patients with audible carotid bruits
- This patient's risk factors of hypertension and hyperlipidemia were well-controlled (lipid panel within normal limits, blood pressure 130/70s during hospitalization without medication).
- Carotid bruits on physical exam was the only sign of critical large-vessel atherosclerosis

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